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Conformational Analysis of MNCB (MBNC) Esters and Amides: Promising Chiral Reagents for Stereoselective Applications

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ABSTRACT: Calculations (MM, AM1/PM3, *ab initio*) and DNMR experiments indicate that 2-(2'-methoxy-1'-naphthyl)-3,5-dichlorobenzoic acid (**MNCB**) and 2'-methoxy-1,1'-binaphthyl-2-carboxylic acid (**MBNC**) esters and amides exist in solution as two conformers in equilibrium: one of them (*sp*) has synperiplanar Ar_1-Ar_2 and C=O bonds, and another one (*ap*) has antiperiplanar bonds.

Due to the close populations of the forms only a part of large shielding effects attributed to the *ap* form is transformed into observed high field shifts in NMR experiments. Thus, the low population of the "*ap*" conformer and the low selectivity of the aryl ring anisotropic influence on the alcohol (amine) moiety are limitations of the efficiency of **MNCB (MBNC)** in their use as reagents for absolute stereochemistry determination of alcohols and amines by NMR. The way to increase the efficiency of this type of reagent has been revealed on the basis of these findings.

INTRODUCTION

The growth of interest in stereoselective synthesis and drug design necessitates effective and reliable methods to control enantiomeric purity and absolute stereochemistry of chiral compounds. Therefore essential efforts have been directed towards developing methods to analyze optically active compounds.[1] Up to now the NMR based method [2] is one of the most attractive ones: it is based on the derivatization of enantiomers (indistinguishable in terms of NMR) into diastereomers by corresponding chiral derivatizing reagents (CDR) followed by analysis of their NMR spectra.

Since the first pioneering work of Raban and Mislow several chiral reagents were proposed and were found to be useful in determination of absolute configuration of secondary alcohols.[3] All of them contain a chiral center and an aryl ring, the asymmetric, anisotropic influence [4] of which in diastereomers leads to the differentiation of esters in NMR. Differences were interpreted using empirical models and rules for determination of absolute configuration were formulated.

Later, in a similar way, several new classes of chiral compounds were studied by NMR: primary and secondary alcohols, primary amines and carboxylic acids.[5]

Recently the main factors that determine the efficiency of the method in the case of secondary alcohols were established and the basic rules for designing new reagents were formulated.[6] It was shown that structures and populations of the main forms are of great importance in this method. New reagents and preferable conditions were proposed on the basis of these findings.

At the same time, during the last years several examples of axially chiral reagent applications were dem-

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